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MEANS OF RECTAL INSTIL-
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BACTERIA AND STRAINS OF
HUMAN BACILLUS COLI
COMMUNIS

BY

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NEW YORK

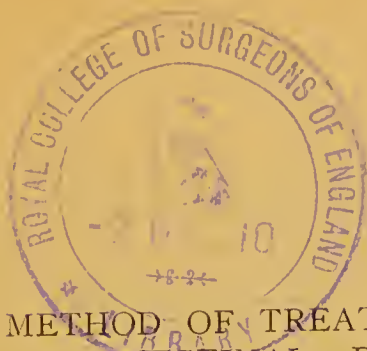
REPRINTED FROM
THE

MEDICAL RECORD

September 24, 1910

WILLIAM WOOD & COMPANY
NEW YORK





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THERE is no doubt that states of chronic intestinal putrefactions are the most numerous of all medical disorders in man. Etiologically the long-established condition is responsible for more permanent types of change of the highly specialized internal organs than all other factors put together, and it is more than probable that future years will show that many of the diseases classed to-day as of obscure origin will be understood to be directly or indirectly due to states of chronic toxemia from the intestinal canal. At the present moment it is evident that many cases of the following are of intestinal origin in their establishment; chronic myocarditis; essential asthma; chronic nephritis; chronic hepatitis; chronic cholangitis, cholecystitis, cholelithiasis; chronic gastric and intestinal atonies; chronic low secretory and motor conditions of the stomach and intestine, and excess sensory condi-

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tions of the first; the mysterious peritoneal and omental adhesions; chronic constipation of dynamic and atrophic origin; chronic colitis, from the simple catarrhal to the membranous and atrophic forms; chronic intestinal indigestion, with fat, sugar, and starch intolerance; arteriocapillary fibrosis, chronic hypertension without sclerosis; premature senility; pseudopernicious anemia, and the true types following gastrointestinal atrophy; chronic simple anemias; gout, intractable neurasthenia; habitual headache; insomnia; catarrhal affections (particularly the general forms with atrophy of the sub-mucous tissues); backache; debility; neuralgias; loss of sexual power; loss of weight and strength; mental confusions; excessive emotional depression and irritability; muscular and mental fatigue; semi-invalidism; vasomotor disturbances; degenerative states of the central and peripheral nervous tissues; functional eye conditions; hypertrophy of the lymphatic tissues; atypical rheumatism, myalgia, and particularly arthritis deformans.

The history of medicine for the treatment of those conditions shows no notable advances until quite recently, when Metchnikoff entered the bacteriology of the subject from a practical standpoint. Before that time a positive excess of indican in the urine established the case as logically one for administration of one of the new intestinal disinfectants or antiseptics (none of which ever were of any practical value) and a few items of general medicine as these seemed to be indicated. Along these lines most of the milder forms of cases improved on the general means of clinical medicine employed, and, caught by the fatus of the literature of the moment on some one of the just advanced intestinal antiseptics, the therapeutic benefits were

attributed to it, and so the controversy for and against the various synthetic proprietary products continued. To-day the care of these cases is about as follows: Following the diagnosis (made mostly from the urine examination), an initial purge is given and the bowels are kept open by some constantly employed drug or enemata, a diet is installed (usually the Bulgarian bacillus milk given, and later on with it also the simple foods), and such general means employed as clinical medicine would suggest.

It is a well-known fact that an individual on a milk diet harbors fewer bacteria in the colon than one on a mixed, a carbohydrate, or a meat diet. The benefits that come from the use of the Metchnikoff milk come from the large amount of lactic acid imbibed, which assists in gastric proteolysis (the normal hydrochloric acid is usually absent or low in the stomachs of these cases) and the milk *per se* taken—not from any practical degree of antagonism between the Bulgarian lactic bacillus with the harmful forms in the intestine. While to a degree this bacterial antagonism is possible of demonstration by laboratory methods, with the results in human beings it is different. Of late I have seen some markedly advanced cases of chronic intestinal putrefaction in individuals who for weeks before had been on this form of milk made according to Metchinkoff's direction, each of whom showed no local or general improvement, the stools from whom yielded from 47 to 83 per cent. of dried weight of bacteria, with a marked preformed sulphate output in the urine, and more than an 8 per cent. loss of milk constituents in the stools.

My interest in the use of a direct bacterial method of treatment was suggested by the uniformity of

the different bacterial pictures seen in examining specimens of normal and abnormal stools stained by the Gram differential method; the fact that the *Coli bacilli* grow only for a certain time in bouillon, when, probably because of their generation of thermostabile and thermolabile substances allied to phenol, their proliferation is inhibited and they become quiescent or resting but not killed (the latter was a confirmation of Conradi and Krupjurveit observations with the *Baccillus coli communis* and the *Bacillus lactis ærognas* (the last of which organism probably suggested the use of the Bulgarian form as a germicidal bacteria against all others); and also, the fact that *Coli bacillus* were most numerous in stools of normal individuals, but were diminished or absent in most cases of excessive chronic intestinal putrefaction, having excess of indican in the urine, even when the intestinal contents have somewhat rapidly passed through the colon. About that time I chanced to read Tissier's Thèse de Paris, 1900, in which he mentioned the inhibitory action of the *Bacillus bifidus* upon the putrefactive anaerobes, the latter being the predominant organisms found in these cases (these are mainly the *B. acrogenes capsulatus* and usually also the Gram negative diplococcus). Shortly following that (1907) Harter's book on bacterial infections of the digestive tract was advanced and in it the various facts pertaining to the germicidal action of the *B. coli* group were compiled, particularly in the following passages, "Nevertheless the evidence now available suggests that in health the colon bacillus, both in man and higher mammals, exerts an important function in combating the development of the injurious saprophytes with which even in health the human intestinal tract almost necessarily abound.

"The presence in the colon of immense numbers of obligate microorganisms of the *B. coli* type may be an important defense of the organism in the sense that they hinder the development of that putrefactive decomposition which, if prolonged, is so injurious to the organism as a whole." "These bacilli are essential to the life of the individual mammal as a defence against bacterial foes which it is impracticable to exclude wholly from the digestive tract, and not as agents in directly facilitating the processes of digestion in the narrow sense." At about this time I confirmed the observation of Herter that the colon bacillus has practically no power to cleave native proteins, that its peptonizing action is slight, and that alone it has not the power to cleave the peptones (and cause the generation of volatile acids, indol, and hydrogen sulphide) unless these have been prepared by peptonization by the other microorganisms. Feeling that the common picture of low amounts of Gram negative bacteria might represent a lowering of the *B. coli* instead of the *B. lactosus aerogenes*, I grew colonies of the stool bacteria from normal and abnormal stools in different media and under different methods, and observed that the abnormal stools generally showed a content of less *B. coli* than the normal stools did. After these observations I perused the literature upon the subject of the *B. coli* by different authors and noted that most of the modern standard works on bacteriology claimed that an immunity against the *B. coli* was not difficult to develop in animals. (Löffler and Abel easily immunized dogs by progressively using subcutaneous doses of live bacteria grown in solid culture and suspended in water; the blood of the immunized animal possessing an active bactericidal

effect upon the colon bacteria, but the serum was not in the correct sense antitoxic.)

Opposed to the above suggestions were many facts arguing against the value of the use of installations of the *Bacillus coli communis* in such cases. The main ones were that a few cases of indolic putrefaction showed larger amount of *B. coli* in the stools than the normal amounts; the fact that the *B. coli* is capable of giving rise to large amounts of indol and indolacetic acid and a rise in the ethereal sulphates in the urine when injected into the duodenum of the dog; the statements of Herter that "muscle fiber or peptones in the lower ileum or large intestine would be attacked by the anaerobes and colon bacilli with a production of indol and subsequent development of indicanuria," and that under conditions of stagnation in the lower part of the ileum where the colon bacilli are numerous "it is not necessary for anaerobes to take part in the attack on the already hydrolyzed protein, since, as repeatedly stated, the colon bacillus itself suffices to do this" (putrefaction), which he proved by experimentation on a healthy dog, and contends is proven by an imperfect action of a cathartic in some persons causing a sudden increase of indican in the urine due to the quick passage of native proteins and peptones from the small into the large intestine where it is possible for the colon bacilli to attack the former; and further in the statement "If the colon bacilli have for any reason ascended in large numbers above their usual upper limit, namely the ileum, into the jejunum or duodenum, they will act there upon peptones formed in the course of the normal digestion of proteins and make indol, and in these instances the aid of the putrefactive anaerobes is not necessary for the production of indol,"

claiming also that if there had been no ascent of the *B. coli* to these regions of the small intestine the putrefactive organisms located there could cleave the proteins and then when the contents had come through the ileocecal valve the *B. coli* in the large gut would cause an abnormal production of indol; and lastly, the significance he gives to the colon bacilli in the production of the indolic form of chronic excessive putrefaction in these words—"the first may be called the indolic type, and is characterized by indicanuria dependent chiefly upon excessive decomposition induced through the co-operation of members of the *B. coli* group."

From the above statements there seemed to be certain arguments in favor and certain ones against use of the rectal instillations of autogenous bacteria and those of the *B. coli* group in the treatment of the conditions under consideration. Nevertheless, encouraged or emboldened by the results recently reported from injections of killed autogenous bacteria in the treatment of other bacterial conditions (notably in the use of the *B. coli* in bacteriuria) I instituted experiments with rectal instillations in a case which had resisted all methods of treatment for months.

The woman was one who showed large amounts of ethereal sulphates in the urine, almost Gram positive stools in which the colon bacilli were few, the stool having an acid reaction in the beginning, the patient displaying a marked anemia, debility, loss of weight, and an established neurasthenia, together with other related symptoms. For the purpose of comparison the medical treatments that had been established before were not changed during the time of injections, and the diet detailed below was continued all of the time, since it seemed a

logical one for such conditions, had been established four months before, and had been closely followed.

From the onset the number of bacteria grown and injected were examined and counted in two groups (Gram negative and Gram positive), and each subsequent stool was also examined before new cultures were inoculated to note any difference in the bacterial picture as time went on. I wish to report this case in full because with certain minor exceptions it answers for the others I have treated since then with the injections of both kinds, and also because the full clinical and laboratory detail of all of the cases would be too long.

Mrs. R. E., married, age 38, born in Russia, the mother of 4 children, had measles 20 years ago. She had no illness until 3 years ago, when she began with pains in the region of the sigmoid (she was pregnant at the time). After the birth of the child she became weak and weaned the infant at the third month. Following this the weakness progressed, she became pale, and was hardly able to attend to her household duties. About a year ago she became unable to do even the lightest domestic work. Then she became markedly pale and nervous, and these symptoms progressed up to the present time. The bowels began to be diarrheal about 10 months ago, and when the diarrhea was severe she had vomiting spells. Often she has had as many as ten fluid movements, accompanied with pain, in one day. These attacks were intermittent. When menstruating she becomes generally worse and has nausea, marked dizziness, and vomiting. Menstruation now very watery and the flow is not steady. The diarrhea is usually worse when menstruating.

She was of an apathetic type, with pale membranes, soft and flabby tissues, normal lungs;

heart, first sound weak and pulse weak with rate of 110; the abdominal walls were thin; there was slight splanchnoptosia. Blood, 3,700,000 erythrocytes. Hb. 67 per cent., leucocytes 7,750; a differential count was not made. On the second day following an Ewald meal, 90 c.c. of material returned which looked well digested, with little mucus, free HCl 17, combined HCl 26, total HCl 43, total acidity 47; the pepsin activity was good and starch digestion was good. The feces were soft and mushy, and their reaction was distinctly acid; examination under low power was negative, excepting that many meat fibers were noted, under high power large numbers of Gram positive bacteria were noted mostly *B. aerogenes capsulatus* and diplococci, Gram negative organisms were few; a watery suspension of 1 to 10 developed 21 per cent. of gas. There was no blood. Segregation cultures showed meager growths of colon bacilli. The urine showed a large amount of indican, a trace of albumin, some hyalin casts, but no glucose. The weight was 113½ lbs.; it was 138 three years ago. Aug. 31 the stool showed large amounts of Gram positive and few Gram negative organisms. It had an acid reaction; the food particles were normal. The urine contained a large amount of indican, a trace of albumin, a few casts, 3.7 grams of sulphate in twenty-four hours; the ratio was preformed sulphates 10, conjugate 4. The treatment included sleep with the windows open, abundant outdoor exercise, a diet as described below, a morning cold sponge, tincture of nux vomica, paregoric and iron; also extract of malt. This treatment was continued for two months with no benefit. The woman was treated from the laboratory from this to the present, the following records

being made: Dec. 27, 1909. Stool, soft, acid reaction, 2 slides of raw feces showing mainly aerogenous bacilli and Gram positive diplococci, but no colon bacilli. Segregation growths showed meager growths of the latter. Dec. 28. Dextrose bouillon: gas result 10 per cent.; very acid media, no indican. Injection 18 c.c. = 738,000,000 Gram positive and very few Gram negative (not more than 700). Urine this day showed marked excess of indican. Dec. 30. Stool much lighter in color than above and not so thin, slightly acid, slides showed large predominance of G. P. but the proportion of G. N. was slightly increased. B. A. C. very prominent and a large number of shorter rodlike non-capsulated organisms were seen, the G. P. diplococci about as before. The B. A. C. were shorter than above and by comparison the bacteria picture of the slides was different from that of 4 days ago.

Jan. 1. Media gas result 25 per cent., no indican formed but some uroresin, reaction of media very acid. Marked change in the bacterial pictures of this bouillon from the foregoing; the G. N. bacteria were more prominent appearing in proportion almost like that seen in normal stools. The B. A. C. were shorter and narrower, and with the G. P. diplococci were not so numerous. The fields of G. N. comprised quite a number of thick clubbed bacilli, but by far more numerous are a thin bacilli which probably are the B. C. C. In a number of fields the proportion between the G. P. and G. N. organisms was about 2 of the former to 1 of the latter. Injection this day of 16 c.c. contained 839,360,000 of G. P. and 460,000,000 of G. N. Much time was spent in the counting. Patient says she is no better, but says that she has not so much cramps in the abdomen. The bowels had not been so loose,

this morning's stool being "quite hard" (one month ago had firm passages for a few days). Her urine still shows much indican, but this was thought to be somewhat less than on all occasions before. Jan. 4. Feces soft and lighter in color than most specimens, reaction amphoteric. Stained specimen shows marked change in bacteria. The reds (G. N.) are more numerous than the violet (G. P.). The B. A. C. are much smaller, more detached, less numerous than in the other specimens, but still are more numerous than in normal stools although they are much shorter than seen in most. There are many quite small G. P. bacilli which looked unlike B. A. C. and around which no capsule could be discerned. The G. P. diplococci were about as found in former specimens. The G. N. were most prominent, being almost 2-3 G. N. diplococci and 1-3 G. N. bacilli. Segregation cultures showed most generous growths of B. C. C. which compared to the results noted from the first specimen of stools showed striking results in the way that the B. C. C. were now much more plentiful in the gut. The picture of this specimen of feces resembled closely the normal stool, and it may be said that if any difference existed it was that there were less G. P. organisms than are ordinarily seen. Jan. 5. Media gas 10 per cent., reaction of fluid acid. Appearance and proportion of G. P. and G. N. organisms about the same as before excepting that the G. N. were greater in number than the G. P. The B. A. C. very scant and still shorter than before. The B. C. C. were somewhat increased in numbers above what is observed in inoculations of normal stools. Injections, 15 c.c. = 120,000,000 G. P. and 165,000,000 G. N. Urine to-day shows decidedly less indican with a sulphate ratio of 10 preformed to

1.7 conjugate. Patient says she feels better which is the first time she has made this statement since coming under observation; she has pains only before defecation, and has had only one stool a day and that formed. Gained 4 lbs. since Jan. 30, two days before the bacterial injections were begun. Jan 7. Feces a rich brown color, medium consistence, reaction amphoteric, foods well digested, red and violet bacteria about evenly divided. B. A. C. normal in numbers (about 3 to a field), G. P. diplococci markedly decreased, B. C. C. plainly evident and in large numbers. Jan. 8. Media, 21 per cent. gas, growth almost level to top of media, fluid very acid, amount 22 c.c. = 1,171,500,000 violet mostly the B. A. C., and 1,405,800,000 reds of the small forms of B. C. C. and a less proportion of long narrow bacilli. Patient says she feels decidedly stronger, has had one formed stool a day and no pain and that she is not as nervous as before. Test for excess indican negative. Blood examination decidedly better and mucous membranes practically normal in color. Jan. 11. Feces rich brown in color and firm in consistence, reaction amphoteric, G. N. and G. P. about equal in numbers, B. C. C. very numerous in all of the fields. G. P. diplococci and B. A. C. apparently increased. Growth on potato showed a thick film of B. C. C. Jan. 12. Media gas result 26 per cent., very acid, fields mostly G. N. bacteria almost all of which are a short rodlike bacilli and some cocci of the B. C. C. group. Fields were seen in which there were as many as 500 organisms and only several G. P. organisms. The B. A. C. apparently were still shorter and not so thick as in the beginning, they comprised practically all the G. P. although here and there was a G. P. diplococci. This speci-

men had the best growth of B. C. C. yet seen, they being present in great predominance and mostly in chains. Injection 19 c.c. = 3,400,000,000 G. N. and 97,000,000 G. P. Urine, indican free. Patient without subjective symptoms excepting still feeling somewhat weak physically but doing all of her housework, including washing and ironing. Gained 3 lbs. more in weight. Patient given a week's interval of injections. Jan. 18. Stool brown color, reaction amphoteric; G. N. and G. P. about equal in numbers. Jan. 19. Media acid, good growth, mostly G. N. but a number of B. A. C. were present, gas 27 per cent. Injection 17 c.c. = 2,100,000,000 G. N. and 970,000,000 G. P. Urine indol free, patient says she had gained 2 lbs. in last 5 days, and that she feels still better and stronger than when last seen. Bowels moved twice to-day without pain, both stools being formed. One week interval of injection. Jan. 25. Stool of rich brown color, reaction amphoteric, more G. P. organisms noted than in last specimen. Jan. 26. Good bacterial growth in media, reaction acid, mostly G. N. but the G. P. were more numerous than in last few. Injection 18 c.c. = 2,900,000,000 G. N. and 1,900,000,000 G. P. Urine has a faint blue indican reaction. Patient says she feels well but had some abdominal pain yesterday and to-day. Conditions not so good as two weeks ago. Ordered to send stool in five days.

Feb. 1. Stool somewhat softer than last specimen, deep brown color, reaction amphoteric, more G. P. present, mostly bacilli but apparently they are not B. A. C. G. P. diplococci very few, G. N. not quite as prominent as before but still in excess of the G. P. Feb. 2. Gas result in media 34 per cent., fields mostly G. N. bacteria but many small

sized G. P. bacilli were noted which probably were not B. A. C. and are of an unknown character, growth fair, injection 15 c.c. = 1,270,000,000 G. N. and 1,100,000,000 G. P. Woman menstruating on this day. Urine indican free. Told to send stool in four days but did not until Feb. 9. Stool normal color but possibly slightly lighter than last one, pasty consistence, reaction amphoteric, G. N. and G. P. about equal in number, the B. A. C. not prominent, the B. C. C. very much so. Feb. 10. Media gas result 37 per cent., growth poor as compared to all former ones, many short rodged G. P. bacilli as before, a few B. A. C. and a large number of G. N. spherical bodies of unknown character growing in groups, injection 17 c.c. = 890,000,000 G. P. and 790,000,000 G. N., most of which latter are B. C. C. Urine indican free this day, and woman had gained 3 lbs. more since last Saturday. Feb. 15. Stool formed and rich brown in color, reaction amphoteric, short rodged G. P. bacilli much fewer, a few B. A. C., G. N. and G. P. about equal in numbers. Feb. 16. Injection 15.5 c.c. = 2,900,000,000 G. N. and 1,500,000,000 G. P., bacterial growths apparently not so prolific as in first medias. Urine indican free, sulphate ratio preformed 10, conjugate 1. Patient says she had one formed and following this one fairly loose movement yesterday but no pain accompanying either or at other times. Patient looks very much improved compared to any time while under observation, is now active and quick in her manner, doing her work each day, and is happy and cheerful. Feb. 26 (ten days since last seen). Stool apparently normal, reaction amphoteric, G. P. and G. N. bacteria about equal in amounts. Only a few B. A. C. seen, but large numbers of B. C. C. Feb. 27. Media less

acid than times before, growth fair. Injection 17 c.c. = 1,300,000,000 G. P. and 1,470,000,000 G. N. Urine indican free. Bowels have moved twice a day for four days, no pain, since last seen had a headache for a few hours on two occasions. Gained 2 lbs. in past week. Weekly injections instituted, bacteria not to be counted, 10 c.c. of media and smaller portions of feces for inoculation to be employed from this on.

Mar. 6. Media growth good, injection 10 c.c. Urine indican free. Patient apparently well. Mar. 13. Media growth fair, injection 10 c.c. Urine indican free. Patient gaining about 2 lbs. in a week. Mar. 21. Media growth fair, injection 10 c.c. Urine faintest trace of indican, sulphate ratio performed 10, conjugate 1.2. Feels well. Mar. 29. Media growth good, injection 10 c.c. Urine indican free. Has gained $5\frac{1}{4}$ lbs. in past four weeks. Stool specimens are about the same in each, G. P. and G. N. organisms about equal in numbers, and the B. C. C. most numerous.

April 5. Media growth good, injection 10 c.c. Urine indican free. April 12. Media growth fair, injection 10 c.c. Urine, faint trace of indican, but uroresin reaction rather marked. April 17. Media growth good, injection 10 c.c. Urine indican free, no uroresin. Patient has gained $17\frac{1}{2}$ lbs. in weight since Dec. 27 (weight now 131) and feels well. Interval of injections now two weeks. Still under observation after six weeks and well, although no injections had been given during this time.

The deductions from this case were that the instillations caused an inhibition to proliferation and a destruction of the *B. aerogenes capsulatus* and the Gram positive diplococci, and a raising to nor-

mal of the *B. coli* in the stools; a sudden change in the reaction of the stools to neutral, and a change in its color and the taking on of a firmer consistence; the stopping of the tendency to diarrhea and the establishing of single daily movements; an elimination of the excess indican in the urine, the sulphate partition ratio diminishing from the preformed 10 to 3.7 conjugate, to 10 preformed to 1 conjugate in six weeks; a most marked improvement in the anemia, general strength and weight of the patient; and lastly an almost permanency of these conditions over months of steady observation, the indican returning in slight excess when the instillations were discontinued for a time and its disappearance again when the injections were again given.

Since that time I have treated twelve cases, none of which had originally responded to the ordinary routine treatments, and all of which patients now have decidedly lessened indican output and all of whom have made substantial general improvement. Nine of these (ten all told) are still under observation, receiving only one injection every two weeks or so and they will be reported again at some subsequent time. The other two have passed from observation but both had indican free urines and were much improved in general health when last seen.

In addition to the above were seven additional cases, four of which were treated with the autogenous mixed injection in the beginning and subsequently with strains of *B. coli communis* obtained from other human beings, and three with the latter from the beginning. In the first four, all of which were treated for at least three weeks with autogenous bacteria, three showed improvement in the way of

a lessened indican output and improved general condition from the autogenous mixed bacteria, but none of whom become indican free, or having near to a normal sulphate ratio. The fourth showed no beneficial change whatever from these injections and is included in the following (which makes four all told) that were treated with strains of *B. coli communis* from the beginning.

The latter were supplied in individual cultures on agar-agar by Dr. William Park from the Health Board Laboratories, were taken originally from the stools of typhoid patients, and were marked "Mary, No. 168, No. 6, No. 171. Brown, No. 3, Mangiuer, and No. 170." The inoculated cultures were first grown for twenty-four hours to get a good surface growth and after this kept in the original tubes at the room temperature, and inoculations were made by placing small loops from each of the tubes into about 15 c.c. of dextrose-bouillon, and the seven strains were grown together for twenty-four hours in the oven at 37°C. when the entire media was injected into the rectum. These injections comprised amounts of the organisms varying in each single injection from 327 millions to 2 billions and the media growths were examined by Gram differential staining and also by growing colonies on the surface of different nutritive medias so as to note if any extraneous bacteria had become inoculated into the original tubes. Up to the time of writing no outside organisms had become mixed with the *B. coli*.

These last seven cases were all those of long standing conditions and may be classed as those that are obstinately resistant to all forms of ordinary treatment. In them other diagnoses of distinct organ affections were easy to be made. These

were, chronic myocarditis in two, chronic nephritis in five, chronic hypertension and arterial sclerosis in five, marked anemia in six and questionable pernicious anemia in one, prolonged neurasthenia in six, premature senility in one, arthritis deformans in one, marked debility and loss of weight and strength in all. The test meal analyses showed that three had gastric subacidity, one an achylia, two a normal secretion and one an excess secretion. In none, however, did the *x*-ray examinations of the colon show any kinks, twists or other types of obstruction, although five of them had varying degrees of prolapse which probably was secondary to the general atony and loss of weight. All but one had habitual constipation, the exception having more or less regularly running diarrheal movements. The stools of each in the beginning showed large amounts of Gram positive organisms and very few Gram negatives, and the urines showed a very dark blue in the chloroform from presence of indican (Stokvis-Jaffe's test with hydrogen peroxide instead of the soda or calcium hyperchloride solution employed), and persistently high conjugate sulphate in the partition from 10 of the preformed to 2.5 to 8 of the conjugate.

With the above mentioned seven cases were two additional ones of like type but which showed high Gram negative stools in the first examination. In these it was believed that the *B. coli* were present in largely increased numbers, and these are not included in the report of the cases for the reasons that they were too few in number, because one had a marked coloptosis and the second an angulation of the transverse colon, and because neither had been under treatment long enough to arrive at any definite conclusions.

The four of the mentioned seven cases that had first been treated with the autogenous mixed injections showed decidedly lessened output of indican in the urine when placed on the strains of *B. coli*, and the development of more equal proportion between the Gram negatives and positives in the stools (usually after about the fifth injection of *B. coli*). But in all a point was reached at which subsequent treatments with the autogenous mixed bacteria seemed to be ineffective although in all relief of symptoms was reported during their course and the benefit in general health was substantial. At the end of the third month of treatment with the autogenous mixed bacteria each was put upon injections of the strains of *B. coli*, and in three an almost immediate further drop in the indican output was noted, the urine eventually becoming almost indican free. The fourth still running an excess but still decidedly decreased indican after the second month of the latter treatment (*in toto* this last case had five months of bacterial treatment). The other two cleaned up completely on the *B. coli*, two inside of ten weeks and the third during the fifth month. The detail of one of the first cases treated with the *B. coli* is the following:

J. W., June 15, 1909, married, age 51, buyer in department store. Had measles and scarlet fever when a child, and diphtheria at 21 years. Had always been constipated but was well and strong up to eight years ago when he contracted typhoid fever. Following this he had a persistent tenderness and pain in the right heel, corresponding to the inner tuberosity of the astragalus which was intensified on walking and deep point pressure and relieved on resting. About three years ago for no known reason to him he became nervous, which condition

manifested itself as a restlessness, lack of power in concentrating his thoughts, an irregular insomnia, some loss of appetite, a more marked constipation, and a steady pain and distressed feeling in the stomach under the left costal arch which was independent of meals and the character and quantity of food. During the first year these general conditions were somewhat intermittent, they being less marked when he was away from business and in the country. In the winter of two years ago he grew gradually worse so that he was unable to attend to business for weeks at a time. In the summer he again picked up in strength and ability to work, but last winter he was unable to attend to business after about Jan. 1, 1909, and since which time he had done nothing in the business way, although he was anxious to. During these three years he had been in the hands of a number of men, and being neurasthenic and impatient hardly gave time enough for any of them to accomplish much in the way of benefit. The diagnoses made were somewhat varied, although "indicanuria" ran pretty generally through them all, and no doubt the treatments installed were good. He said that he made the most improvement in the physician's hands just before me who give him extract of malt and cascara segrada, a meat free diet, and ten drops of tincture of nux vomica at his meals. However, after about a month he failed to make further progress and although changes in the treatment were made said that he "could feel himself slipping back again."

Examination: weight 149 lbs. (weight 205 three years ago); has a pallid countenance and pale mucous membranes; muscles soft and his skin flabby; nervous, apprehensive and excitable; had a

hemic blow over the base of the heart; a marked gastric spash and an enlarged stomach; fecal masses in the sigmoid and descending colon; exaggerated knee jerks; an arterial pressure of 170 m.m. Hg.; and a marked amount of indican in the urine (almost a blue black). Ewald meal (June 17) return 95 c.c.; finely subdivided starch; no blood, lactic acid, or Boas-Oppler bacilli; free HCl 0, combined HCl 11, total acidity 19; starch digestion to maltose marked. Feces (when four days on the test foods), dark color and acid reaction; muscle fibers numerous, some striated; large masses of vegetable substances; thick coating of mucus on surface of stool; typical Gram positive stool, showing many B. A. C. and G. P. diplococci, and but very few G. N. bacteria and not more than one or two G. N. bacilli to a field. Urine, 1,400 c.c. Sp. Gr. 1.021; acid; trace of albumin; indican and uroresin reaction marked; sulphates 4.2 grams, ratio sulphates 4 conjugate to 10 preformed; urea 31 grams; moderate number of hyalin and granular casts, some renal and many squamous cells and a few cylindroids. Blood, 3,100,000 erythrocytes, 6,900 leucocytes, Hb. 64 per cent.

From June 17 to Nov. 11, 1909, various treatments were employed with only fair and most times discouraging results. The agar-agar established daily movements of his bowels within the first week of treatment, and this regularity was maintained up to the present. He seemed to make the most improvement on excessive amounts of outdoor exercise (walking seven miles a day), morning rubs with a towel soaked in cold water, the diet, and tincture nux vomica 10 in liq., ferri albuminatis 100, taking two teaspoonfuls after meals in water. During these

five months some improvement was noticed in his general condition; the best blood count was on September 17, when 4,100,000 erythrocytes and 7,200 leucocytes were counted and 77 per cent. of Hb. But on all occasions largely increased amounts of indican in his urine were observed (39 examinations), the albumin and casts persisting. At times when it was believed that the patient was substantially better (particularly one time when he returned from a two weeks' sojourn in the country) a total sulphate examination of the urine was made with a ratio sulphate, and even on this occasion the sulphate output was 4.1 grams and the ratio was 3.7 conjugate and 10 preformed. On one occasion the arterial tension was 135 m.m.Hg., but at all other times it was higher; about half of the times it was around the figure first mentioned and in a few instances it was above. The man continued to feel weak, look poorly, was unable to work, and he constantly complained of the gastric pain or distress. The examination of his stools on three occasions showed the acid reactions and high G.P. and very few G.N. organisms. It was believed in November that no better results in the way of controlling the excessive intestinal putrefaction were possible by medical means, and that only a fair degree of benefit was possible from medical treatments and then only when these were constantly kept up over lengths of time. Encouraged by the success in clearing a case just before with instillations of the strains of *B. coli*, but which case had discontinued observation when the urine had cleared and the stools had improved in character, I began these treatments in the case, continuing also the diet, morning rubs, long walks, and the tonics with the following results:

November 15, dextrose-bouillon, 15 c.c., good

growth, no indol in media, and reaction acid, injection 374,000,000 B.C.C. November 19, media 16 c.c., good growth, acid reaction, no indol in media, injection 327,000,000 B.C.C. November 23, media 15 c.c., growth good, acid reaction, injection 395,000,000 B.C.C. Patient's urine shows less indican to-day than ever before; says he feels somewhat stronger and slept better. November 27, media 17 c.c. and reaction, growth good, injection 410,000,000 B.C.C. Patient gained 2 pounds in last twelve days. November 30, media 16 c.c., gas result 70 per cent., media acid, trace of indol, growth good, injection 405,000,000 B.C.C. Patient says he feels that he is getting better; his urine shows only the faintest trace of indican.

December 3, specimen of stool submitted to-day shows neutral reaction, about $1/3$ G.N. to $2/3$ G. P. bacteria and very few B.A.C. Media 14.5 c.c., acid reaction, growth fair, injection 315,000,000 B.C.C. Patient gained 3 pounds in last six days, appetite is much better, and the gastric distress has stopped. December 6, media 15 c.c., growth fair, and reaction acid, injection 270,000,000 B.C.C. Urine faint trace of indican and no uroresin. December 10, media 14 c.c., growth good, bacteria not counted. December 16, media 15 c.c., acid reaction, injection 347,000,000 B.C.C. No indican shown in urine test. Blood count 4,700,000 erythrocytes, 7,900 leucocytes, Hb. 84 per cent. Patient looks well and says he feels much better. Injection once a week. December 22, media 19 c.c., growth good, bacteria not counted. Urine indican free. December 29, media 15.5 c.c., acid reaction, growth good, injection 410,000,000 B.C.C. Has had no distress in his stomach all of this month, gained 9 pounds in weight since November 27.

January 8, media 17 c.c. and reaction marked, growth good, bacteria not counted. Urine shows a trace of indican. Yesterday had eaten rather large quantities of meat at two meals. January 15, Media 16 c.c., growth good, acid reaction, bacteria not counted. January 22, media 17 c.c., growth fair, bacteria not counted. Urine free of excess indican. January 29, media 15 c.c., growth fair, bacteria not counted. Gained $7\frac{1}{2}$ pounds in a month.

February 8, stool examination: The G.N. and G.P. equal in numbers, few B.A.C. seen, reaction neutral. Media 16 c.c., bacteria not counted. Injection at 10-day intervals. February 18, media 18 c.c., acid reaction, bacteria not counted. Injection at two-week intervals.

March 4, media 17 c.c., bacteria not counted. Has gained 6 pounds since Jan. 29, and looks much improved and of good color. March 18, media 16 c.c., bacteria not counted, urine indican free. Ewald test meal 67 c.c., return F. HCl 27, combined 21, total HCl 48, total acidity 53. March 22, media 16.5 c.c., bacteria not counted. Patient has resumed his work, feeling strong and active. Urine indican and albumin free, but still has casts.

April 3, media 15 c.c., growth good, bacteria not counted. Arterial tension 125 m.m.Hg. April 16, media 17 c.c., growth good, bacteria not counted. Urine indican free. Continuing steadily at his work and nervousness gone. Says he feels as of old.

Treatments continued at time of writing excepting at three-week intervals. Patient well.

This was an ideal case of chronic intestinal putrefaction of the gut due to the G.P. anaerobes with elimination of the G.N. organisms, in which the results from the medical treatments continued over five months' time were only fair, and in which the

fecal instillations of the *B. coli* obtained from other human beings gave signal results both in the general way and in the reestablishment of the proper proportions between the G.N. and G.P. organisms in the gut. As the latter was brought about, the amount of indican in the urine with the total sulphate output and the ratio between the preformed and conjugate sulphates became normal. The man was brought from a debilitated, anemic neurasthenic unable to work to one that appeared normal in every way. A further interesting fact was the differences in the two test meal analyses (made nine months apart) in which it appeared that the toxins from the gut depressed the digestive secretions, and that when these toxins were no longer generated in excessive amounts the stomach secretion returned to normal. The blood pressure also came down to a figure that may be considered as safely normal and has remained at these lower figures.

The diagnoses of the excessive putrefactive condition in the gut were made by noting the various general or organ conditions with an initial examination of the urine for indican. The condition suggested, a purge was given (calomel and salts or castor oil), and when the bowels had moved well, carmine or lampblack was given to demarcate the stools and the patients were placed upon the following test diet.

"The diet mentioned below is to be strictly adhered to for three or four days. The stools of the first thirty-six hours after its institution are of no value for examination. If constipation exists, the bowels are to be moved by injection at the end of the thirty-six hours. After this time, providing the bowels have moved well, the entire first stool is to be sent as soon as possible, no purges being taken

in the meantime. Fresh specimens are desirable, and a covered small tin can or glass jar can be used as a container. The output of urine of twenty-four hours should accompany the specimen of stool.

"Diet.—Morning: Two thin slices of well-baked bread with butter liberally supplied; one pint of oatmeal gruel, made of about $1\frac{1}{2}$ oz. or 40 gm. of oatmeal; $\frac{1}{4}$ oz. or 10 gm. of butter; 6 oz. or 200 gm. of milk; $8\frac{1}{2}$ oz. or 300 gm. of water, and one egg (strained).

"11 A. M.: Milk, 1 pint or 500 c.c.

"Noon: A good-sized piece of steak or roast beef chopped or cut into very fine pieces (about 4 oz. or 125 gm.) and served on a slice of toast; one bowl (about 8 oz. or 250 gm.) of mashed potatoes with $\frac{1}{4}$ oz. or 10 gm. of butter.

"4 P. M.: Milk, 1 pint or 500 c.c.

"Night: Same diet as breakfast."

The specimen of urine was examined for indican and uroresin, and a sulphate partition was made, close attention being paid to the ratio between the preformed and conjugate sulphate. When the chromogens were markedly increased in the urine and the urine showed a ratio partition between the two sulphate combinations of more than 10 of the preformed to 1 of the conjugate a specimen of stool was examined. The reaction of this was taken, the color noted, examination of the surface layer made when it was formed not when it was of soft consistence, and a portion of the center was examined between slides with the low power to note the appearance of food crystals, etc. Seven and a half grams of the stool were macerated in 25 c.c. of sterile water and fermented and the gas result noted, and slides were made of portions of the interior of the stool, these

being stained by the Gram differential method. In the latter, attention was paid to the character of the gross proportion of the Gram positive and Gram negative bacteria. When the latter were low, a tube closed at one end was filled with dextrose bouillon and inoculated. The bacteria grown in twenty-four hours was examined and comparison of these latter slides were made with those of the raw stool before so as to note the differences in the bacterial pictures and also if the Gram negatives had a tendency to increase in number when grown in culture. If such was the case, the autogenous mixed bacteria was employed, if not the *B. coli* medias were employed. These were grown in about 15 c.c. of dextrose bouillon for twenty-four hours at 37° C., at which time an examination was made of the bacterial result, and the organisms counted in classes of Gram positives and Gram negatives, or just the *B. coli* when these only were used. In some instances where doubt existed as to the character of the organisms, colonies were grown on potato and on bouillon gelatin. When the bacterial instillations were instituted close attention was paid to the clinical side of the case, the weight was taken regularly, the red cells counted and the Hb. estimated from time to time, differences in the examination of the stools and bacterial inoculation results from them were noted in all instances. Altogether, the observation covered an immense field of laboratory labor and observation, at times discouraging, but in the end most grateful.

The medical treatments that had been used before the instillations were begun were usually stopped, although when tonics, enemata, etc., were indicated they were utilized more or less although not as steadily as had been the case before. Outdoor exer-

cises, regular hours of sleep, morning cold sponges and other hygienic details were kept up, and also this diet.

"General Rules.—Care should be taken that all foods are fresh and cleanly cooked and served. The mouth should be cleansed with plain warm water before and after partaking of food and when possible at other times. All raw fruits should always be peeled. Drink a glass of warmed flaxseed water before meals. Foods should not be eaten during conditions of fatigue, mental excitement or depression, and a rest after each meal is desirable. Thorough mastication of the food is important, and such foods as can be mashed on the plate should be so treated. The vegetables and cereals should be well cooked, and condiments, such as pepper, mustard, lemon, etc., are not allowed. Not much food should be eaten at any one time; smaller meals and shorter intervals are more desirable. Kefir, Kумыс, Matzoon, and peptonized milk are the only forms in which milk can be used.

"Foods allowed. Bouillon, consommé, broths, and purées. Well-cooked rice, tapioca, farina, sago, oatmeal, and hominy and served with milk, sugar, and fresh cream. Eggs in any form and not taking more than two in a day. Bread, rolls, swieback, toast, biscuits, and crackers. All foods made with gelatin, both the animal and vegetable form. If constipated take a handful of agar-agar finely cut once a day with cream. Take as much fresh butter, fresh cream, and olive oil as possible. Beef, lamb, chicken, sweetbreads, liver, etc., and fish can be eaten in small quantities once a day, providing they are fresh, roasted, or broiled, and taken in a finely comminuted form (their use in made up dishes is not allowed). All of the vegetables can be taken.

but they must be cooked to softness; peas, beans, lentils are wholesome. The green vegetables and salads are also beneficial. When constipation is severe and the bowels do not move with the agar-agar a dish of stewed prunes sweetened with milk sugar instead of cane sugar should be taken each night before retiring. Custards, egg and milk, cereal or fruit, jellies, marmalade, stewed fruits are allowable. Other foods of value are apples, pears, brown bread, rice, barley, black grapes, potatoes, carrots, asparagus, green chicory, cabbage, and spinach."

From the results achieved I have come to the following conclusions: In cases of chronic intestinal putrefaction wherein such conditions as carcinoma, colonic obstruction, abnormal organic disease of the pancreas or stomach, or gastrointestinal atrophy, etc., are not responsible for the condition, much benefit can come from raising the content of *B. coli communis* in the gut by instillation either of the autogenous mixed forms or strains from other individuals; whether this is due to a real antagonism between the toxins of the *B. coli* and the other putrefactive organisms, these toxins being existant in the cultures injected (which bacteriologists claim is slight in amount with the *B. coli*), or whether the *B. coli* so injected are directly toxic to these other bacteria I am not prepared to say. (We know that the dead as well as the living *B. coli* are very toxic.) But it is certainly true that an individual who has high Gram positive stools can by the autogenous mixed or *B. coli* instillations quickly have the running proportion between the Gram negatives and positives raised to a proportion equivalent to normal, this being due to a raising in the *B. coli* and also to a diminution in the putrefactive Gram positives as the first become more

numerous. With this more equal proportion between the two types of organisms, the conjugate sulphate of the urine diminishes and the cases make substantial improvement in the general body. Whether this raising of the Gram negatives is only due to the *B. coli* or only to the *B. lactosus aerogenes* (both being antitoxic to other bacteria), or to both together, is not always possible of determination, since both are much alike in their morphology and are Gram negative in character. But the cultural methods of distinguishing these two forms from each other and the results obtained when only the *B. coli* were used in the injections incline me to believe that these disorders are due to a shortage or inactivity of the *B. coli*, and that the latter are the most powerful agents in the human alimentary canal against the development of putrefactive conditions, and, that while outside of the intestine they are destructive and pyogenic, inside of the canal they are welcome hosts. From my experiences I am led to believe that these injections are a valuable method for treating these cases, quick and effective in the great majority, and not harmful in any. It is my belief that when anatomic conditions causing stagnation exist the results from these treatments are not capable of giving such good or substantial benefit. As regards the permanency of the benefit brought about it is apparent that about half of the cases which do not respond to simple treatments clear up inside of from one to three months of this treatment, but that the other half may not remain substantially benefited even when the instillations are kept up for longer periods. These latter show relapses when the instillations have been stopped for a week or more, quickly responding again when the injections are reestablished and some eventually clear up.

It is probable that in the relapsing cases some permanent anatomical mischief preventing the establishment of a normal bacterial intestinal condition is present, which is either the cause of the development of the condition in the first instance and then its prolongation, or that there is present some anatomical or permanent functional change affecting normal secretions and motility of the digestive canal in asthenic ways. All cases of putrefactive conditions should first be treated by the routine methods of treatment for those conditions (diet, hygiene, tonics, etc.) before instituting the instillations. When, however, the latter are begun, the autogenous mixed bacteria should first be used, always employing fresh specimens of stools for inoculation of the media and this treatment kept up for about four weeks before a change to the strains of *B. coli* is employed for a length of time, and when benefit had been established a return to the autogenous mixed bacteria may be used. If no benefit is noted on the *B. coli* alone the *B. lactosus aerogenes* may also be added to them, the two grown together in the single media, and these tried for a length of time. And if after these no sustained or apparent benefit is achieved then we have present some anatomic and permanent complication affecting the function of the gut, and the best we can hope for is a resort to surgery in some of the cases, or a longer interval continuation of instillations of whatever form of culture has shown the best results in that particular case.

The bacteria were all grown under identical conditions, namely, in about 15 c.c of 2 per cent. dextrose bouillon for twenty-four hours at 37° C., when the entire media was injected. This was done after an enema of normal saline solution to cleanse the

lower bowel, the patient being on the left side and remaining so for 15 minutes after the instillation. The routine was one injection every fourth day until benefit was noted, and after this at longer intervals, the treatment being kept up for months if necessary.